A Randomized Phase III Study to Assess the Effect of a Longer Duration of Consolidation Treatment With Nilotinib on TFR in CP CML (ENESTPath)

This study is currently recruiting participants. (see Contacts and Locations)

Verified August 2015 by Novartis

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT01743989

First received: December 4, 2012
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History of Changes

Purpose

This study aims to assess the optimal duration of nilotinib 300 mg BID consolidation treatment, in order that patients remain in treatment-free remission (≥MR4.0) 12 months after starting the Treatment-Free Remission (TFR) phase of the study.

Rationale:

CP-CML patients who have received 2 or more calendar years of first-line imatinib treatment, and who have failed to achieve the molecular response threshold for treatment cessation (≥MR4.0) have a 50% greater chance of doing by switching to nilotinib; however the optimal duration of consolidation treatment with nilotinib to ensure the highest rate of patients remaining in ≥MR4.0 after entering the TFR phase is not yet known. This protocol therefore aims to assess the potential impact of a longer duration of consolidation treatment with nilotinib, i.e. 12 months versus 24 months, on molecular relapse rate in the first 12 months of treatment-free remission.

Condition	Intervention	Phase
Leukemia, Myeloid, Ph1-Positive	Drug: Nilotinib	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: A Prospective, Randomized, Open Label, Two Arm Phase III Study to Evaluate Treatment Free Remission (TFR) Rate in Patients With Philadelphia-positive CML After Two Different Durations of Consolidation Treatment With Nilotinib 300mg BID

Resource links provided by NLM:

Drug Information available for: Nilotinib

Genetic and Rare Diseases Information Center resources: Chronic Myeloproliferative Disorders

U.S. FDA Resources

Further study details as provided by Novartis:

Primary Outcome Measures:

- optimal duration of consolidation treatment with nilotinib 300 mg BID to ensure the highest rate of patients remaining in ≥MR4.0 12months after entering the TFR phase. [Time Frame: 48 months] [Designated as safety issue: No]

the primary endpoint is the number of patients w ho remain in treatment free remission (≥MR4.0) ,w ithout molecular relapse, at the end of 12 months in the TFR phase of the study, in the nilotinib 12 months consolidation treatment arm (arm 1) versus the nilotinib 24 months consolidation treatment arm (arm 2).

Secondary Outcome Measures:

- To evaluate the proportion of patients w ho are eligible to suspend nilotinib therapy by achieving and maintaining a sustained ≥MR4.0 for at least 12 months during consolidation treatment w ith nilotinib 300 mg BID [Time Frame: 12 months] [Designated as safety issue: No]

  The proportion of patients w ho have achieved a sustained ≥MR4.0 (defined as having 4 out of 5 quarterly assessments of ≥MR4.0 by a EUTOS standardized laboratory over the last 12 months and the last assessment before randomization is at least MR4.0) during the consolidation treatment phase of the study.

- The kinetics of the molecular response in patients during induction/consolidation treatment w ith nilotinib 300 mg BID. [Time Frame: 24 or 36 months depending on randomized arm] [Designated as safety issue: No]

  The proportion of patients w ho achieve MR4.0 or MR4.5 on the study at selected time points during the induction/consolidation phase of the study.

- The kinetics of the molecular response in patients during the TFR phase of the study in the tw o treatment arms. [Time Frame: 36months (arm1); 24 months (arm2)] [Designated as safety issue: No]

  The proportion of patients w ho maintain in MR4.0 or MR4.5 on the study at selected time points during the TFR phase in each one of the tw o treatment arms

- Progression-free survival (PFS) rate during the TFR phase of the study. [Time Frame: 36 months (arm1); 24 months (arm2)] [Designated as safety issue: Yes]

  PFS defined as progression to AP/BP or death, w here the "failure" event is the earliest occurrence of either of these events; Kaplan-Meier (KM) estimation of PFS is measured from the date of start of the nilotinib TFR phase to the date of the earliest failure event. Patients not know n to have recurred or died on or before the cut-off date for the KM analysis w ill have their PFS interval censored at the earlier of the date of their last assessment (cytogenetic, hematology or extramedullary) for patients w ho are still on study, and at the date of last contact for patients w ho are in follow -up.

- Treatment -free survival (TFS) during the TFR phase of the study [Time Frame: 36 months (arm1); 24 months (arm 2)] [Designated as safety issue: Yes]

  TFS is defined as lack of any of the follow ing events: loss of MMR, confirmed loss of MR4.0, re-start of nilotinib treatment, progression to AP/BP, or death from any cause;KM estimation of TFS, w hich is measured from the date of the start of the nilotinib TFR phase to the date of the earliest of the follow ing: loss of MMR, confirmed loss of MR4.0, re-start of nilotinib treatment, progression to AP/BP, or death from any cause.

- Overall survival (OS) rate during of the TFR phase of the study. [Time Frame: 36 months (arm1); 24 months (arm2)] [Designated as safety issue: Yes]

  Overall survival is defined as the time from start of the TFR phase to the time of death due to any cause. For patients w ithout any event on or before the cut-off date, survival time w ill be censored at the date of their last assessment for patients w ho are still on study, and at the date of last contact for patients w ho are in follow -up -

- Safety profile of nilotinib during the induction/consolidation treatment phase, the TFR phase, and during the treatment re-initiation phase. [Time Frame: 60 months] [Designated as safety issue: Yes]

  Descriptive statistics on adverse events, laboratory abnormalities and clinically notable ECG and other safety parameters during the study

Estimated Enrollment:	1058
Study Start Date:	April 2013
Estimated Study Completion Date:	July 2020
Estimated Primary Completion Date:	July 2020 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Active Comparator: arm 1 12 months of nilotinib consolidation (arm 1) plus 36 months of TFR phase	Drug: Nilotinib Nilotinib w ill be provided to patients for at least 24 or 36months. (depending if nilotinib re-initiation is necessary- nilotinib w ill be provided during nilotinib re-initiation phase)

Active Comparator: arm 2 24 months of nilotinib consolidation plus 24 months of TFR phase	Drug: Nilotinib Nilotinib w ill be provided to patients for at least 24 or 36months. (depending if nilotinib re-initiation is necessary- nilotinib w ill be provided during nilotinib re-initiation phase)

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Key Inclusion Criteria:

- Confirmed diagnosis of chronic phase Ph+ CML
- Previous first-line treatment w ith imatinib for a minimum of 2 years;
- Patient in complete cytogenetic response;

Key Exclusion Criteria:

- Previous achievement of MR4.0 at study entry;
- Previous treatment w ith other target cells inhibitors other than imatinib;
- Patients w ith any history of detectable atypical Leukemia transcripts or patients w ith detectable atypical leukemia transcripts at screening;
- Previous anticancer agents for Chronic myeloid leukemia other than imatinib except for cytoreduction;
- Severe and/or uncontrolled concurrent medical disease that in the opinion of the investigator could cause unacceptable safety risks or compromise compliance w ith the protocol;
- History of other active malignancies w ithin the 5 years prior to study entry w ith the exception of previous or concomitant basal cell skin cancer and previous carcinoma in situ treated curatively;
- Patients w ho have not recovered from prior surgery;
- Treatment w ith other investigational agents w ithin 4 w eeks of Day 1;
- Impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of study drug;

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk w ith your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below . For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT01743989

Contacts

Contact: Novartis Pharmaceuticals +41613241111

Contact: Novartis Pharmaceuticals

Show 342 Study Locations

Sponsors and Collaborators

Novartis Pharmaceuticals

Investigators

Study Director: Novartis Pharmaceuticals Novartis Pharmaceuticals

More Information

No publications provided

Responsible Party: Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier: NCT01743989 History of Changes
Other Study ID Numbers: **CAMN107AIC05**, 2012-005124-15
Study First Received: December 4, 2012
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Health Authority:	Belgium: The Federal Public Service (FPS) Health, Food Chain Safety and Environment Czech Republic: State Institute for Drug Control Denmark: Danish Medicines Agency Estonia: The State Agency of Medicine Finland: Finnish Medicines Agency France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) Germany: Federal Institute for Drugs and Medical Devices Greece: National Organization of Medicines Latvia: State Agency of Medicines Lithuania: State Medicine Control Agency - Ministry of Health Norw ay: Directorate of Health Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products Portugal: National Pharmacy and Medicines Institute Slovak Republic: Ethics Committee Slovenia: Agency for Medicinal Products - Ministry of Health Spain: Agencia Española de Medicamentos y Productos Sanitarios Sw eden: Medical Products Agency United Kingdom: Medicines and Healthcare Products Regulatory Agency Italy: The Italian Medicines Agency Bulgaria: Bulgarian Drug Agency Croatia: Agency for Medicinal Product and Medical Devices Hungary: National Institute of Pharmacy Romania: National Medicines Agency Serbia and Montenegro: Agency for Drugs and Medicinal Devices Austria: Federal Office for Safety in Health Care European Union: European Medicines Agency

Additional relevant MeSH terms:

Leukemia, Myelogenous, Chronic, BCR-ABL Positive	Leukemia
Leukemia, Myeloid	Myeloproliferative Disorders
Bone Marrow Diseases	Neoplasms
Hematologic Diseases	Neoplasms by Histologic Type

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